REMARKS

Formalities

Claim 57 has been amended. Claim 70 has been canceled. The amendment does not add or constitute new matter, and is completely supported by the application as originally filed. Support may be found throughout the specification and in the originally filed claims. Specifically, support for the amendment to claim 57 may be found, for example, at page 55, line 17 through page 63, line 28, of the specification.

The amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in related applications. Moreover, the amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. The Applicants reserve the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation or continuation-in-part application.

Upon entry of the amendment, claims 57-69 and 71 are pending in the instant application.

Objection to the Specification

The Examiner has maintained the objection to the specification regarding the allegedly contradictory phenotypes of the heterozygous mice described by the Applicants. Specifically, the Examiner has stated that the specification discloses that the heterozygous mutant mice exhibit both increased fasting blood glucose levels and decreased fasting blood glucose levels. The Examiner asserts that with evidence in the specification to support the allegedly contradictory phenotypes, "it cannot be determined which phenotype(s) the mice actually displayed". Applicants respectfully disagree with the Examiners conclusions, and have attempted to explain the distinct circumstances under which the contradictory evidence was observed. Specifically, the decreased fasting glucose levels were observed in serum or plasma after fasting. Fasting plasma or serum glucose measurements are a typical way to measure and compare blood glucose. Decreases in this glucose measurement were observed in heterozygous mutant mice in two different examples described in the specification. First, reduced serum glucose levels were observed in heterozygous mice during routine serum chemistry panel screening (see, *e.g.* page 58, lines 9-10). A second example of decreased serum/plasma levels observed after a five-hour fast immediately prior to a glucose tolerance test. Evidence in the specification supporting decreased or reduced serum glucose levels is more compelling than the statement referred to by the Examiner describing increased glucose

levels. However, Applicants realize that the status of the instant Office Action is final, and therefore have overcome the objection by 1) canceling claims relating to or encompassing the heterozygous mutant mice, or 2) amending claims to recite or encompass only the homozygous disruption and phenotypes corresponding to the mice whose genome comprise the homozygous disruption. More particularly, the pending claims recite transgenic mice whose genomes comprise homozygous disruption of the endogenous glucagon receptor, which exhibit phenotypes including a metabolic abnormality or a pancreatic abnormality. These claims no longer encompass the heterozygous mouse. Therefore, it is believed that this objection is no longer relevant.

Rejections

The Examiner has rejected claims 57-71 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse the rejection. However, in light of the amendment to claim 57 and the cancellation of claim 70, this rejection is no longer relevant.

In one aspect of the rejection, the Examiner states that the specification does not provide adequate guidance for determining the existence of or function of mouse glucagon receptor genes other than that described in the specification. The Examiner states, "[d]eleting the word 'an' preceding the term "endogenous" in claims 57 and 70 would overcome this rejection." Applicants have adopted the Examiner's suggested modification for claim 57, and claim 70 has been canceled, rendering this aspect of the rejection moot.

In another aspect, the Examiner asserts that the specification fails to enable making the transgenic mice comprising homozygous and/or heterozygous disruption of the glucagon receptor gene which exhibit any phenotype other than those disclosed in the specification. As a basis for this aspect of the rejection, the Examiner states that the claims encompass both homozygous and heterozygous mutant mice, but recite only the phenotypes of the homozygous mice, and therefore encompass a heterozygous mouse exhibiting any phenotype. Applicants have amended the claims, in particular parent claim 57, in order to recite a transgenic mouse whose genome comprises a "homozygous" disruption in the endogenous glucagon receptor gene, wherein the transgenic mouse exhibits a metabolic abnormality or a pancreatic abnormality. These claims no longer encompass the transgenic mouse comprising a heterozygous disruption in the glucagon receptor gene, and are

fully enabled by the instant specification. Therefore, Applicants have overcome this aspect of the rejection with regards to claim 57, and its dependents, including claims 58-69 and 71.

With regard to claim 70, the Examiner asserts that the claim encompasses a transgenic mouse whose genome comprises a homozygous disruption in an endogenous glucagon receptor gene wherein the mouse has any phenotype. The Examiner states that "the phenotype of reduced fertility... is the phenotype of the offspring of the claimed mouse and does not reflect any observable or detectable phenotype of the claimed mouse..." Applicants respectfully disagree. The phenotype of reduced fertility refers to the transgenic mouse whose genome comprises a homozygous disruption in the glucagon receptor gene recited in this claim in that this mouse is unable to produce offspring. This is a characteristic of the claimed mouse, and is supported by the instant disclosure. However, in order to place the claims in condition for allowance, this claim has been canceled without prejudice.

The Examiner states that claim 71 falls under this rejection as it depends from claim 70. However, claim 71 recites a cell obtained from the transgenic mouse of claim 57, namely the transgenic mouse whose genome comprises a homozygous disruption in the glucagon receptor gene and exhibits a phenotype including a metabolic abnormality or a pancreatic abnormality. Therefore, in light of the amendment to claim 57 to recite only the homozygous disruption and its corresponding phenotype, it is believed that this rejection has been overcome as it applies to claim 71.

It is believed that the claims are in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-1271 under Order No. R-648.

Respectfully submitted,

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